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A case report of the new Polyzene™-F COBRA PzF™ Nanocoated Coronary Stent System (NCS): Addressing an unmet clinical need☆

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ABSTRACT

Because of anticipated antiplatelet medication risks, patients who are not DES candidates or who are at particularly high risk for bleeding events have been targeted initially for treatment with the COBRA PzF Coronary Stent System. We report the case of a successful experience with a new, Polyzene™-F COBRA PzF™ Coronary Stent System, designed to impart thrombo-resistance and reduce inflammation, to achieve shorter dual antiplatelet therapy duration while reducing restenosis incidence in a high risk patient with atrial fibrillation.

1. Introduction

Even with the use of new-generation drug-eluting stents (DES), stent thrombosis and major adverse cardiac and cerebrovascular events (MACCE; composite of death, myocardial infarction or stroke) continue to be clinical risks associated with coronary stent placement. Mitigation of these risks is accomplished with consideration of the patient's comorbidities and stent selection. Typically, stent choice requires pharmacologic antiplatelet medication for a minimum of 1 month of dual antiplatelet therapy (DAPT; combination of ASA and a P2Y12 inhibitor) post bare metal stent (BMS) placement or for a minimum of 6–12 months DAPT after placement of a drug-eluting stent (DES) per ACCF/AHA/SCAI 2011 PCI and ESC/EACTS 2014 Guidelines on elective percutaneous coronary intervention (PCI) [1,2,3].

Patients treated for atrial fibrillation (AF) are at additional risk when undergoing PCI. Combining chronic oral anticoagulation (OAC) therapy with DAPT, resulting in triple antithrombotic therapy, has been and continues to be intensely scrutinized. Prevention of thromboembolic (stroke) and atherothrombotic (stent thrombosis) events is balanced against the increase risk of severe bleeding in all, but in particular, the triple therapy patients [4]. Careful deliberation includes reducing the duration of or eliminating one or more antithrombotic medications as well as consideration of alternative stent designs for patients at higher risk of bleeding events.

A middle ground in stent design, available through use of Polyzene™-F nano-coating, is designed to impart thrombo-resistance and reduce *in-situ* inflammation. This coating on the COBRA PzF™ Coronary Stent System offers a compromise position by shortening DAPT duration to one month with the potential of reducing restenosis incidence. Patients who are not DES candidates or who are at higher risk for bleeding events have been targeted initially for treatment with the COBRA PzF Coronary Stent System and this report provides a description of one of the first uses of the device system with its special properties.

2. Case report

A 72-year-old female with a history of significant comorbidities, including atrial fibrillation, angina (CCS III), arterial hypertension, heart failure, hyperlipidemia, diabetes mellitus type 2 and history of ischemic stroke, was diagnosed with a 75% stenotic mid-LAD lesion; see Fig. 1.

Additional risk assessments included a CHA_2DS_2-VASc score of 7, which is associated with a 9.6% per year risk of stroke without warfarin treatment [5,6], and a HAS-BLED score of 4, which is associated with a 4.9%–19.6% one year bleeding risk while on oral anticoagulants [7]. This particular subject's specific, but not atypical, profile places her at significant bleeding risk so appropriate stent selection was critical. In April 2014, she received a cobalt chromium alloy COBRA PzF Stent with Polyzene™-F nano-coating (CeloNova BioSciences, Inc., San Antonio, Texas). The COBRA PzF Stent (CE marked) is indicated for improving coronary luminal diameter in patients with symptomatic ischemic heart disease due to coronary artery lesions and is intended for use in patients eligible for percutaneous transluminal coronary angioplasty (PTCA, PCI) with reference vessel diameter of 2.5–4.0 mm.

Abbreviations: AF, atrial fibrillation; BMS, bare metal stent; DAPT, dual antiplatelet therapy; DES, drug-eluting stent; MACCE, major adverse cardiac and cerebrovascular events; MI, myocardial infarction; OAC, oral anticoagulation; PCI, percutaneous coronary intervention; PTCA, percutaneous transluminal coronary angioplasty.

☆ Conflict of interest: Prof. S. Silber, MD and P. Styllou, MD have no relevant conflicts of interest.

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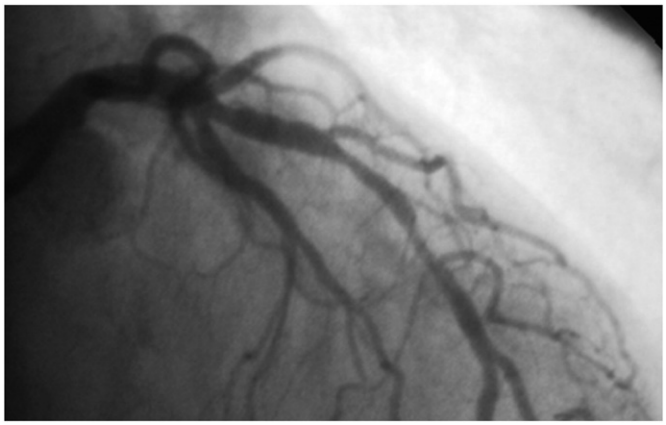

Fig. 1. Baseline image is depicted of a 75% stenotic mid-LAD lesion in a female with multiple co-morbidities, including atrial fibrillation, arterial hypertension, heart failure, hyperlipidemia, diabetes mellitus type 2 and history of ischemic stroke.

With 5F guide catheter compatibility and low (0.89 mm) crossing profile, due in part to the thin (71 μm) struts, the COBRA PzF stent proved its deliverability. Stent delivery and deployment were unremarkable and the stent's radiopacity permitted an appreciation of full apposition within the target vessel; see Fig. 2.

2.1. Medical therapy

Post-procedure antiplatelet therapy consisted of clopidogrel (75 mg) and acetylsalicylic acid (100 mg) daily for 4 weeks. Due to atrial fibrillation, phenprocoumon, a coumarin vitamin K antagonist, was administered, targeting an INR of 2.0–2.5, during the same 4 week period, after which rivaroxaban (20 mg), a direct factor Xa inhibitor, was prescribed daily. The modification in anticoagulation regimen from phenprocoumon to rivaroxaban after 4 weeks was made on the patients' desire to avoid INR controls and require as few tablets as possible. This anticoagulation regimen may also have a reduction of hemorrhagic infarcts [8]. Aspirin was stopped after 4 weeks, in accordance with the consensus document [9]. No medication compliance concerns were noted.

2.2. Follow-up

To date, the patient has not experienced any adverse or serious adverse events. Assessments have been made, including clinic visits and ECGs, in-hospital and at 30, 180 and 270 days post-procedure. The patient has reported a decrease in symptoms and increased physical activity has been observed.

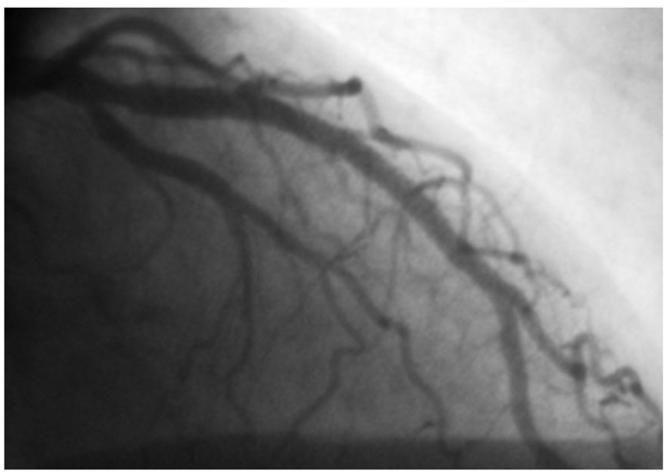

Fig. 2. The final result of the deployment of the cobalt chromium alloy COBRA PzF Stent with Polyzene™-F nano-coating is depicted and full apposition within the vessel is noted.

3. Discussion

Many clinicians agree that use of a BMS, where possible, limits triple therapy duration by restricting DAPT to one month [10]. Conversely, current thinking suggests DES selection increases the duration of triple therapy to 3–6 months. However, with the use of the COBRA PzF™ Coronary Stent System, DAPT can be limited to one month but the restenosis incidence falls in line with a DES.

Stent selection is based on thorough risk assessment of factors each individual presents, coupled with attributes and characteristics of the intended stent. Each device has an inherent risk/benefit profile when factoring the best course of action for a particular patient's comorbidities and anatomy. The decision between implantation of a BMS, DES or, a bioabsorbable stent, whose scaffold is absorbed after 1–2 years, has included a concomitant cocktail of antithrombotic pharmacologic agents and their respective duration of administration, in the determination.

With its ultra-thin F nano-coating (≤0.05 μm) of Polyzene(TM) on a cobalt chromium alloy, thin strut stent platform, the COBRA PzF Coronary Stent, designed to provide flexibility, stability and support, offered the patient described in this report a successful clinical balance of stent selection and DAPT duration. While the stent coating is approximately 100 times thinner than typical DES coverage, the Polyzene™-F material has demonstrated decreased platelet adherence and aggregation [11,12], while decreasing inflammation and facilitating re-endothelialization [13]. In the longer term, the surface material has been reported to decrease neointimal proliferation, late loss and restenosis rate [13,14,15,16]. Researchers have speculated that albumin's preferential binding to Polyzene™-F provides favorable conditions for stent strut endothelialization. This observation is thought to be responsible, in part, for the positive clinical results seen with Polyzene-F material on the Catania™ stent in the ATLANTA and ATLANTA 2 studies that demonstrated a 3.6% clinically-driven target lesion restenosis rate, with no deaths, strokes or myocardial infarctions (MIs), in 55 patients and 6.5% all target lesion restenosis rate in 300 patients with 0% late stent thrombosis (>30 days) recorded at 12 months in both studies [15,16]. With respect to atherothrombotic events, it has been shown that an increased risk of late stent thrombosis is associated with a morphometrically determined ratio, *i.e.*, uncovered to total struts per section [17]. An optical coherence tomographic comparison, within the same patients, of stent endothelialization showed greater coverage on the Polyzene-F coated struts at 7–10 days and at 28–32 days post implantation when compared to DES and BMS struts and a lower uncovered to total strut ratio for the Polyzene-F coated stents at all time points, except when it was not different from the DES struts at the later time point [18,19].

Reduction of antithrombotic medications associated with the use of the COBRA PzF™ Coronary Stent System, both in the decrease of duration and elimination of multiple pharmacologic agents can be further appreciated when reflecting on a large scale, nationwide, retrospective registry on 40,812 patients diagnosed with a first-time MI [20]. Bleeding incidence, defined as a hospital admission with a diagnosis of non-fatal bleeding (primary or secondary) or a diagnosis of bleeding as the cause of death (fatal bleeding), was 2.6% for the ASA group, 4.6% for clopidogrel, 4.3% for vitamin K antagonist, 3.7% for ASA plus clopidogrel, 5.1% for ASA plus vitamin K antagonist, 12.3% for clopidogrel plus vitamin K antagonist, and 12.0% for triple therapy. When the data were normalized, using aspirin as a reference value of 1, adjusted hazard ratios for bleeding risk were 1.33 (95% confidence interval 1.11–1.59) for clopidogrel, 1.23 (0.94–1.61) for vitamin K antagonist, 1.47 (1.28–1.69) for ASA plus clopidogrel, 1.84 (1.51–2.23) for aspirin plus vitamin K antagonist, 3.52 (2.42–5.11) for clopidogrel plus vitamin K antagonist, and 4.05 (3.08–5.33) for triple therapy. Selection of the antithrombotic agents, alone and in combination, is clearly an important consideration in reducing bleeding risk.

In a more current, prospective, double-blind, placebo-controlled, phase III trial, 15,526 patients within 7 days of acute coronary syndrome were randomly assigned (1:1:1) to receive twice daily doses of either 2.5 mg or 5 mg of rivaroxaban or placebo for a mean of 13 months [21]. Both doses of rivaroxaban reduced the primary efficacy composite endpoint, death from cardiovascular causes, MI or stroke, as compared with placebo. However, for subjects with atrial fibrillation, only the lower dose of rivaroxaban resulted in an increased survival benefit. In part, this finding was explained by the authors due to the increase in fatal bleeding associated with the higher dose of rivaroxaban.

As is typical in patients with significant coronary artery disease and atrial fibrillation, the patient who is the subject of this manuscript was required to undergo triple therapy, based on her CHA_2DS_2-VASc score of 7 and a HAS-BLED score of 4, she was at high risk for embolic and bleeding events. However the duration of her triple therapy medication regiment was limited to one month, which lowered the bleeding risk for this patient. DAPT duration and oral anticoagulation have to be considered carefully and be as short as possible. The dosages of 2.5 mg or 5 mg b.i.d of rivaroxaban are based on the ATLAS ACS 2-TIMI 51 trial. This trial studies patients with ACS and how rivaroxaban reduces cardiovascular death, MI, or stroke in patients following ACS, and cannot be extrapolated to patients with atrial fibrillation and stable CAD. The patient in this manuscript had no ACS, normal renal function and takes NOAC at a dose of 20 mg daily due to atrial fibrillation.

4. Conclusion

Because of anticipated antiplatelet medication risks, patients who are not DES candidates or who are at particularly high risk for bleeding events have been targeted initially for treatment with the COBRA PzF Coronary Stent System. The particular patient described in this report is an ideal example of the initial intended clinical population for the COBRA PzF Stent and describes how the new stent design and materials serve this currently unmet clinical need. Because of various comorbid factors, stent selection was critical to the initial and long term clinical results seen with the COBRA PzF Stent. Planned clinical investigations of the stent are needed to establish the clinical utility of the device.

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Disclosure

The COBRA PzF Stent System is an investigational device and not approved for sale in the United States, however, it is available for sale in countries accepting CE marked devices.

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References

[1] Levine GN, Bates ER, Blankenship JC, et al. 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions [published correction appears in *Circulation*. 2012;125(8):e412]. Circulation 2011;124(23):e574–651.
[2] Windecker S, Kolh P, Alfonso F, et al. Authors/Task Force members. 2014 ESC/EACTS Guidelines on myocardial revascularization: the Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS), developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI). Eur Heart J 2014;35(37):2541–619.
[3] January CT, Wann L, Alpert JS, et al. 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol 2014;64(21):2246–80.
[4] Sourgounis A, Lipiecki J, Lo TS, Hamon M. Coronary stents and chronic anticoagulation. Circulation 2009;119:1682–8.
[5] Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the Euro Heart Survey on atrial fibrillation. Chest 2010;137(2):263–72.
[6] Olesen JB, Lip GY, Hansen ML, et al. Validation of risk stratification schemes for predicting stroke and thromboembolism in patients with atrial fibrillation: nationwide cohort study. BMJ 2011;342:d124–33.
[7] Pisters R, Lane DA, Nieuwlaat R, de Vos CB, Crijns HJ, Lip GY. A novel user-friendly score (HAS-BLED) to assess one-year risk of major bleeding in atrial fibrillation patients: the Euro Heart Survey. Chest 2010;138(5):1093–100.
[8] Ruff C, Giugliano RP, Braunwald E, Hoffman EB, Deenadayula N, Ezekowitz MD, et al. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials. Lancet 2014;383:955–62.
[9] Lip GY, Windecker S, Huber K, Kirchhof P, Marin F, JM Ten Berg, et al. Management of antithrombotic therapy in atrial fibrillation patients presenting with acute coronary syndrome and/or undergoing percutaneous coronary or valve interventions: a joint consensus document of the European Society of Cardiology Working Group on Thrombosis, European Heart Rhythm Association (EHRA), European Association of Percutaneous Cardiovascular Interventions (EAPCI) and European Association of Acute Cardiac Care (ACCA) endorsed by the Heart Rhythm Society (HRS) and Asia-Pacific Heart Rhythm Society (APHRS). EUR Heart J 2014;35(45):3155–79.
[10] Welle A, Grunze M, Tur D. Plasma protein adsorption and platelet adhesion on poly[bis(trifluoroethoxy)phosphazene] and reference material surfaces. J Colloid Interface Sci 1998;197(2):263–74.
[11] Mrowietz C, Franke RP, Seyfert UT, Park JW, Jung F. Haemocompatibility of polymer-coated stainless steel stents as compared to uncoated stents. Clin Hemorheol Microcirc 2005;32:89–103.
[12] Satzl S, Henn C, Christoph P, et al. The efficacy of nanoscale poly[bis(triflouroethoxy) phosphazene] (PTFEP) coatings in reducing thrombogenicity and late in-stent stenosis in a porcine coronary artery model. Invest Radiol 2007;42:303–11.
[13] Virmani R. In-vivo vascular response study and acute swine shunt model study. Euro PCR Programme; 2013. p. 21–4 [Paris].
[14] Tamburino C, La Manna A, Di Salvo ME, et al. First-in-man 1-year clinical outcomes of the Catania Coronary Stent System with nanothin Polyzene-F in de novo native coronary artery lesions. The ATLANTA (Assessment of The LAtest Non-Thrombogenic Angioplasty stent) Trial. J Am Coll Cardiol 2009;2(3):197–204.
[15] Tamburino C, Capodanno D, Di Salvo ME, et al. Safety and effectiveness of the Catania Polyzene-F coated stent in real world clinical practice: 12-month results from the ATLANTA 2 registry. EuroIntervention 2012;7(9):1062–8.
[16] Finn AV, Joner M, Nakazawa G, et al. Pathological correlates of late drug-eluting stent thrombosis: strut coverage as a marker of endothelialization. Circulation 2007; 115(18):2435–41.
[17] La Manna A, Capodanno D, Cera M, et al. Optical coherence tomographic results at six-month follow-up evaluation of the Catania Coronary Stent System with nanothin Polyzene-F surface modification (from the Assessment of The LAtest Non-Thrombogenic Angioplasty Stent [ATLANTA] trial). Am J Cardiol 2009;103(11):1551–5.
[18] Tamburino C, Capodanno D, La Manna A, di Salvo M, Sanfilippo A, Prati F. Rapid Evaluation of Vessel HEaling After AngiopLasty (REVEAL) trial: rationale, objectives and design. J Cardiovasc Med (Hagerstown) 2010;11(1):53–8.
[19] Sørensen R, Hansen ML, Abildstrom SZ, et al. Risk of bleeding in patients with acute myocardial infarction treated with different combinations of aspirin, clopidogrel, and vitamin K antagonists in Denmark: a retrospective analysis of nationwide registry data. Lancet 2009;374:1967–74.
[20] Mega JL, Braunwald E, Wiviott SD, et al. Rivaroxaban in patients with a recent acute coronary syndrome (ATLAS ACS 2-TIMI 51). N Engl J Med 2012;366:9–19.
[21] Paikin JS, Wright DS, Crowther MA, Mehta SR, Eikelboom JW. Clinician update: triple antithrombotic therapy in patients with atrial fibrillation and coronary artery stents. Circulation 2010;121:2067–70.